



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,674	02/14/2002	Kenneth K. Sokoll	1151-4172	1691
27123	7590	07/23/2008		
MORGAN & FINNEGAN, L.L.P. 3 WORLD FINANCIAL CENTER NEW YORK, NY 10281-2101			EXAMINER LE, EMILY M	
			ART UNIT	PAPER NUMBER
			1648	
			NOTIFICATION DATE	DELIVERY MODE
			07/23/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTOPatentCommunications@Morganfinnegan.com
Shopkins@Morganfinnegan.com
jmedina@Morganfinnegan.com



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/076,674
Filing Date: February 14, 2002
Appellant(s): SOKOLL, KENNETH K.

Maria C. H. Lin
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 19, 2008 appealing from the Office action mailed August 10, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

This appeal involves claims 1, 4-9, 12-13 and 18-19.

Claims 2-3 and 11 have been canceled.

Claims 10, 14-17 and 20-75 are withdrawn from consideration as not directed to the elected invention or species.

Appellant failed to properly list claim 10 as withdrawn. Claim 10, as noted in the previous office actions, has been withdrawn from examination for being directed to a non-elected species. While it is noted that in response to the initial withdrawal of claim 10 from examination, see final office action mailed 08/10/2007, Appellant argues that that claims to non-elected species are not considered withdrawn. See 2nd paragraph, page 13, Appellant's after final amendment, filed 12/17/2008. However, as communicated to Appellant in the mailed advisory action before the filing of an appeal brief, contrary to Appellant's argument, claims that are not directed to elected species are considered withdrawn for its merits are not being examined.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The Claims Appendix is substantially correct. The minor error(s) is as follows:
Claim 10 should be listed as withdrawn for reason(s) set forth in the advisory action before the filing of the appeal brief and readdressed at item **(3) Status of Claims**.

(8) Evidence Relied Upon

WO 01/22972	Krieg et al.	04-2001, publication date
WO 94/25060	Ladd et al.	11-1994, publication date

Result no. 1 of the rng and result no. 1 of the rag search summary pages, cited by the Office, 02/17/2005.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

1. Claims 1, 5, 7-9, 12-13 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg et al.¹ in view of Ladd et al.,² as evidenced by result no. 1 of the rng and result no. 1 of the rag search summary pages.

The claims are directed at composition that is a microparticulate comprising a cationic peptide immunogen and an anionic CpG oligonucleotide. The claims require the peptide immunogen to comprise a target B cell antigen or a CTL epitope and a T helper cell epitope; have a net positive charge at a pH in the range of 5.0 to 8.0, which is calculated by assigning a +1 charge for each lysine, arginine and histidine; a -1 charge for each aspartic acid and glutamic acid; and a charge of 0 for all other amino acids in the cationic peptide immunogen. The claims require the anionic CpG oligonucleotide have a net negative charge at a pH in the range of 5.0 to 8.0; and be single-stranded DNA comprising 8 to 64 nucleotide bases with a repeat of a cytosine-guanidine motif, wherein the number of repeats of the CpG motif is in the range of 1 to 10.

Claim 5, which depends on claim 1, requires the net positive charge of the synthetic peptide immunogen be at least +2. Claim 7, which depends on claims 5 and 6, in the alternative, requires the net negative charge of the anionic oligonucleotide be at least -2. Claim 8, which depends on claim 1, further requires the CPG oligonucleotide to be 18-48 nucleic acids residues in length, and have 3 to 8 repeats of

¹ Krieg et al. WO 01/22972.

Art Unit: 1645

a cytosine-guanidine motif. Claim 9, which depends on claim 1, requires the CpG oligonucleotide to have the formula: $5'X^1CGX^23'$, wherein X^1 is selected from the group consisting of A (adenine), G (guanine) and T (thymine); and X^2 is selected from the group consisting of C (cytosine) and T (thymine). Claim 12, which further limits claim 1, and claim 13, which depends on claim 12, specify that the nucleic acid sequence of the CpG oligonucleotide is SEQ ID NO: 1.

Claim 18, which depends on claim 12, requires the cationic peptide immunogen be a synthetic peptide that is conjugated to a T helper cell epitope. Claim 19, which depends on claim 18, specifies that the amino acid sequence of the cationic peptide immunogen is SEQ ID NO: 9.

Prior to the obviousness analysis, the following is observed:

It is noted that the nucleic acid sequence of SEQ ID NO: 1 is $5'TCGTCGTTTTGTCGTTTTGTCGTTTTGTCGTT-3'$, which is a single stranded DNA of 32 nucleic acid residues in length having 5 repeats of a cytosine-guanidine motif, and has a net negative charge of -32 at a pH in the range of 5.0-8.0. In the instant, the number of cytosine-guanidine repeats is with the range that is instantly claimed, 1-10 and to 3-8. The number of nucleotide bases present in SEQ ID NO: 1 is within the 8-64 and 18-48 ranges set forth in the claims. SEQ ID NO: 1 is also in agreement with the formula $5'X^1CGX^23'$, wherein X^1 is selected from the group consisting of A (adenine), G (guanine) and T (thymine), and X^2 is selected from the group consisting of C (cytosine)

² Ladd et al. WO 94/25060.

and T (thymine). And SEQ ID NO: 1 has a net negative charge of at least -2 , as required by the claims.

SEQ ID NO: 9 is a cationic peptide immunogen comprising a CTL epitope and a T helper cell epitope, has a net positive charge of $+4$, and is synthetic peptide immunogen conjugated to a T-helper epitope.

Krieg et al. teaches a composition comprising an immunostimulatory nucleic acid and an anti-cancer therapy. [See claim 99] One of the immunostimulatory nucleic acid Krieg et al. teaches is an anionic CpG oligonucleotide. The anionic CpG oligonucleotide that Krieg et al. teaches has the sequence set forth in SEQ ID NO: 429. [Claim 101, and item 429 on page 46.] SEQ ID NO: 429 of Krieg et al. is 100% identical to the SEQ ID NO: 1 set forth in the claims. [See result no. 1 of the rmg search summary page.] Thus, SEQ ID NO 429 of Krieg et al. is a single stranded DNA of 32 nucleic acid residues in length having 5 repeats of a cytosine-guanidine motif, and has a net negative charge of -32 at a pH in the range of 5.0-8.0. In the instant, the number of cytosine-guanidine repeats is with the range that is instantly claimed, 1-10 and to 3-8. The number of nucleotide bases present in SEQ ID NO: 429 of Krieg et al. is within the 8-64 and 18-48 ranges set forth in the claims. SEQ ID NO: 429 of Krieg et al. is also in agreement with the formula $5'X^1CGX^23'$, wherein X^1 is selected from the group consisting of A (adenine), G (guanine) and T (thymine), and X^2 is selected from the group consisting of C (cytosine) and T (thymine). And SEQ ID NO: 429 of Krieg et al. has a net negative charge of at least -2 .

And by anti-cancer therapy, Krieg et al. intends to encompass immunotherapeutic agents. [Lines 1-4 of page 15] In the instant, it is not readily apparent if the immunotherapeutic agents that Krieg et al. teaches are cationic peptide immunogens comprising a CLT epitope and a T helper cell epitope. However, Ladd et al. teaches an immunotherapeutic agent that is a cationic peptide immunogen comprising a CLT epitope and a T helper cell epitope. Ladd et al. refers to this cationic peptide immunogen as SEQ ID NO: 35. SEQ ID NO: 35 is 100% identical to SEQ ID NO: 9 set forth in the claim. [See result no. 1 of the rag search summary page.] Thus, SEQ ID NO: 35 of Ladd et al. is a cationic peptide comprising a CTL epitope and a T helper cell epitope, has a net positive charge of +4, and is synthetic peptide immunogen conjugated to a T-helper epitope.

Ladd et al. teaches that the cationic peptide immunogen is useful for regulating infertility and for treating prostatic hyperplasia, androgen-dependent carcinoma, prostatic carcinoma and testicular carcinoma in males. Ladd et al. also teaches that the cationic peptide immunogen is useful for treating endometriosis, benign uterine tumors, recurrent functional ovarian cysts and premenstrual syndrome, and preventing or treatment of estrogen-dependent breast cancer in females. [Abstract]

Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to combine the teachings of Ladd et al. and Krieg et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to treat prostatic hyperplasia, androgen-dependent carcinoma, prostatic carcinoma and testicular carcinoma in males; and treat endometriosis, benign

uterine tumors, recurrent functional ovarian cysts, premenstrual syndrome, and prevents or treats estrogen-dependent breast cancer in females. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Ladd et al. demonstrates that the immunotherapeutic agent identified as SEQ ID NO: 35 is useful for treating prostatic hyperplasia, androgen-dependent carcinoma, prostatic carcinoma and testicular carcinoma in males; and treating endometriosis, benign uterine tumors, recurrent functional ovarian cysts, premenstrual syndrome, and prevents or treats estrogen-dependent breast cancer in females.

2. Claims 1, 4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg et al. in view of Ladd et al., as applied to claim 1 above.

Claim 4, which depends on claim 1, requires the cationic peptide immunogen be a mixture of synthetic peptide immunogens. Claim 6, which further limits claim 4, requires the average net positive charge of the mixture of synthetic peptide immunogen to be at least +2.

The significance of Krieg et al. and Ladd et al., as it pertains to claim 1, is provided above.

In addition to teaching a cationic peptide immunogen having the same amino acid as that of SEQ ID NO: 9 recited in the claims, Ladd et al. also teaches the use of a mixture of synthetic peptide immunogens. Specifically, Ladd et al. teaches a mixture comprising the cationic peptide immunogen identified as SEQ ID NO: 35 with SEQ ID NO: 10. [Claim 20 of Ladd et al.] Furthermore, Ladd et al. also suggests the use of one

Art Unit: 1645

or more peptide immunogens to reduce or suppress LHRH levels in a mammal. [Lines 26-35 of page 30]

Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use a mixture of peptide immunogens. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to obtain an efficient immune response toward the reduction or suppression of LHRH levels in a mammal. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the determination of a workable, optimal or efficient condition is routinely practiced in the art.

Additionally, a mixture of synthetic peptide immunogens having the amino acid sequence of SEQ ID NOs: 10 and 35 would yield a net positive charge of at least +2. SEQ ID NO: 35 has a net positive charge of +4. SEQ ID NO: 10 has a net positive charge of also +4. The average of the two charges is at least +2.

(10) Response to Argument

At paragraph bridging pages 6-7 of Appellant's brief, Appellant argues that Krieg et al. does not teach or disclose the word "anionic" or the phrase "net negative charge".

Appellant's argument has been considered, however, it is not found persuasive. While Krieg et al. does not expressly uses the word "anionic" nor the phrase "net negative charge", the absence of such usage does not equate to a lack of teaching by Krieg et al. In the instant case, Krieg et al. teaches of immunostimulatory oligonucleotides. The oligonucleotides of Krieg et al. are inherently anionic and thus,

Art Unit: 1645

have a net negative charge for it is well known in the art that oligonucleotides are anionic and have a net negative charge. Additionally, as pointed out in the rejection, Krieg et al. teaches an oligonucleotide comprising CpG motif that is the same as those encompassed by the claimed invention and recited in claim 13. Claim 13, which depends on claim 12, which depends on independent claim 1, requires that the CpG oligonucleotide encompassed by claims 1 and 12 be SEQ ID NO: 1. SEQ ID NO: 1 is 5'TCGTCGTTTTGTCGTTTTGTCGTTTTGTCGTT-3'. Krieg et al. teaches SEQ ID NO: 429. SEQ ID NO: 429 of Krieg et al., as evidenced by result no. 1 of the rng search summary page, is 100% identical to claimed SEQ ID NO: 1. In the instant case, the fact that Krieg et al. teaches an oligonucleotide that is the same as those claimed clearly establishes a prima facie case that Krieg et al. teaches an "anionic" oligonucleotide that has a "net negative charge".

At pages 7-8 and second paragraph, page 11 of Appellant's brief, Appellant argues that Krieg et al. does not teach a cationic peptide. Appellant also argues that Krieg et al. does not teach complexing the anionic oligonucleotide with anti-cancer therapeutic agents because Krieg et al. teaches putting the oligonucleotide in one container and the anti-cancer therapeutic agents in another container. Appellant cited lines 19-26, page 18 of Krieg et al. to support Appellant's argument.

Appellant's argument has been considered, however, it is not found persuasive. Appellant is reminded that the rejection is an obviousness rejection over Krieg et al. in view of Ladd et al. Had Krieg et al. teaches a cationic peptide, Krieg et al. would have been cited as anticipating the claimed invention. However, because Krieg et al. does

Art Unit: 1645

not teach a cationic peptide, Krieg et al. has been cited as rendering the claimed invention obvious in view of the teachings of Ladd et al. In the instant case, while Krieg et al. does not teach a cationic peptide, Krieg et al. clearly teaches that oligonucleotides comprising CpG motifs are immunostimulatory. Krieg et al. also clearly teaches using oligonucleotides comprising CpG motifs as an adjuvant in vaccines and anti-cancer therapeutic agents, including immunotherapeutic agents to enhance the immune response induced by the vaccines and immunotherapeutic agents. Krieg et al. clearly suggests the use of oligonucleotides comprising CpG motifs as adjuvants in vaccines and immunotherapeutic agents. And, at the time the invention was made, Ladd et al. teaches of an immunotherapeutic agent. The immunotherapeutic agent that Ladd et al. teaches is a cationic peptide. The cationic peptide of Ladd et al. has 100% identity to the cationic peptide claimed, and specifically recited in claim 19. The cationic peptide of Ladd et al., which Ladd et al., designates as SEQ ID NO: 35 is the same as claimed SEQ ID NO: 9, which is recited in claim 19. Hence, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to combine the teachings of Krieg et al. and Ladd et al. for the reason(s) set forth in the rejection. Moreover, Appellant is reminded that *KSR* forecloses argument that specific teaching, suggestion or motivation is required to support a finding of obviousness. *KSR*, 82 USPQ2d at 1396. That is, Krieg et al. does not have to specifically teach or suggest a "cationic peptide" to render the claimed invention obvious. In the instant case, it is clear from the teachings of Krieg et al. that oligonucleotides comprising the CpG motifs has

immunostimulatory activities and can be used as adjuvants in vaccines or immunotherapeutic agents.

Regarding Appellant's assertion that Krieg et al. does not teach complexing the oligonucleotide with anti-cancer therapeutic agents, it appears that Appellant has taken the teachings out of its intended context. Lines 19-26, page 18 of Krieg et al. is directed at a kit for the composition suggested by Krieg et al., an oligonucleotide comprising a CpG motif with an anti-cancer therapeutic agent. The cited passage is limited to a kit. Additionally, contrary to Appellant's argument, Krieg et al. does teach a composition that comprises the oligonucleotide and an anti-cancer therapeutic agent. The Office directs Appellant's attention to lines 13-15, page 18 of Krieg et al.

Additionally, it is noted that at page 8 of the brief, Appellant submits that Krieg et al. is not concerned with the stability of the peptide immunogens or recognize to stabilize peptide immunogens. To support Appellant's position, Appellant notes that Krieg et al. discloses the use of phosphodiester oligonucleotides comprising CpG motifs as producing maximal effect, whereas, Appellant's specification, page 27, discloses that the phosphodiester bond is unstable and the phosphodiester group may be modified to a phosphorothioate group.

Appellant's submission has been considered, however, it is not found persuasive. In the instant case, it is not readily apparent as to the relevance of such submission. The claims are not limiting to the type of backbone, either phosphodiester or phosphorothioate, that the oligonucleotide must possess. In the instant case, Appellant's claimed invention encompasses oligonucleotides that have either

Art Unit: 1645

phosphodiester or phosphorothioate backbones. Additionally, contrary to Appellant's implied assertion that Krieg et al. does not teach that phosphodiester bond is unstable and the phosphodiester group may be modified to a phosphorothioate group. The Office directs Appellant attention to lines 1-19, page 36 of Krieg et al. At the cited passage, Krieg et al. clearly teaches the modification of the natural phosphodiester backbones to phosphorothioate backbones or chimeric thereof. Krieg et al. teaches that oligonucleotides comprising the CpG motif having the modified backbone of phosphorothioate provide maximum activity and protect the nucleic acid from degradation by intracellular exo- and endo-nucleases. In the instant case, Krieg et al. clearly teaches stabilization of the oligonucleotides via modifying the backbone linkages.

At page 8, Appellant also argues that Krieg et al. does not teach or provide any guidance on how to modify the oligonucleotide if it were not anionic. Specifically, Appellant argues that Krieg et al. does not disclose, teach or suggest a method of rendering CpG oligonucleotide anionic by modifying the oligonucleotide with a phosphorothioate group.

Appellant's arguments have been considered, however, it is not found persuasive. Contrary to Appellant's assertion, Krieg et al. does teach modifying the oligonucleotide with a phosphorothioate group. The modification taught by Krieg et al. is discussed in the above paragraphs. Additionally, it should be noted that Krieg et al. teaches of oligonucleotides, which are inherently anionic and have a net negative charge. Thus, it is unclear as to why Appellant is alleging that Krieg et al. does not

teach modifying the oligonucleotide with a phosphorothioate group when Krieg et al. clearly teaches the use of phosphorothioate backbones to stabilize the oligonucleotide. Additionally, because oligonucleotides are inherently anionic, it is unclear why Krieg et al. has to teach modifying the oligonucleotide to have a phosphorothioate backbone to render it anionic. Moreover, the arguments presented herein by Appellant contradict Appellant's disclosure. At paragraph [0037], page 15 of the Appellant's specification, Appellant clearly discloses that the natural phosphodiester backbone has a negative charge. Thus, if the natural phosphodiester backbone has a negative charge, then it is unclear as to why Appellant asserts that a modification of the phosphodiester backbone to a phosphorothioate backbone is necessary to render a negative charge.

At first paragraph, page 9, and third through fourth paragraphs, page 11 of brief, Appellant criticizes the Office for arriving at a net negative charge of -32 at pH in the range of 5.0 to 8.0 for claimed SEQ ID NO: 1, which has 100% identity to SEQ ID NO: 429 of Krieg et al. Appellant also argues that to a person of ordinary skill in the art, each nucleic acid residue is neutral and has a negative charge of zero. Appellant also argues that it would defy scientific principles to be able to form a stable immunogen with 16 to 32 cationic peptides to one CpG oligonucleotide. Appellant notes that Appellant has indicated a +2 charge for the cationic peptide is preferred.

Appellant's criticism has been noted. The calculation of a net negative charge of -32 is in accordance with the teachings of Appellant's disclosure. At paragraph [0037], page 15 of the Appellant's specification, Appellant teaches that each phosphodiester or phosphorothioate group present in the oligonucleotide is assigned a charge of -1. In the

instant case, claimed SEQ ID NO: 1 has 32 nucleic acids, which renders 32 phosphodiester or phosphorothioate group, hence a net negative charge of -32.

Regarding Appellant's assertion that to a person of ordinary skill in the art, each nucleic acid residue is neutral and has a negative charge of zero, it appears that Appellant has inadvertently confused nucleobases/nucleosides with nucleic acids and nucleotides. Nucleic acids are linear polymers consisting of repeating nucleotide units, wherein each nucleotide consists of three components, a phosphate ester, a pentose sugar and a heterocyclic base. The heterocyclic base is a nucleobase. A nucleoside is a nucleobase attached to a pentose sugar. In the instant case, because nucleotides has a phosphate ester group attached to it, wherein the natural phosphate ester group is phosphodiester, which has a assigned charge of -1, it is inherently anionic. In the case of nucleobase and nucleosides, neither has a phosphate ester group attached, it is inherent neutral, has a net charge of zero.

With regard to Appellant's argument that it would defy scientific principles to be able to form a stable immunogen with 16 to 32 cationic peptides to one CpG oligonucleotide, such has been noted, however, it is not found persuasive. It is unclear as to what Appellant is directing at with such assertion. The claims are not directed at forming a stable immunogen with 16 to 32 cationic peptides to one CpG oligonucleotide. The claims are not specific as to the number of cationic peptides that should be complexed with each oligonucleotide. It should be noted that in the instant case, Krieg et al. teaches an anionic oligonucleotide comprising the CpG motif, wherein the oligonucleotide of Krieg et al. has the same sequence as the claimed oligonucleotide,

Art Unit: 1645

and Ladd et al. teaches a cationic peptide that has the same sequence as the claimed cationic peptide. Thus, if Appellant asserts that the combination defies scientific principles, then, perhaps an enablement rejection against Appellant's claimed invention would be more appropriate. In the instant case, it is found that Appellant's arguments are not consistent with Appellant's disclosure. Appellant teaches complexation between SEQ ID NO: 1, which has 100% identity to SEQ ID NO: 429 of Krieg et al., and SEQ ID NO: 9, which has 100% identity to SEQ ID NO: 35 of Ladd et al. Moreover, Appellant's disclosure demonstrates that complexation between an anionic oligonucleotide and cationic peptide is formed spontaneously. See [0082], page 29 of Appellant's specification.

Regarding Appellants notes that Appellant has indicated a +2 charge for the cationic peptide is preferred, it should be noted that the most limiting claims are directed to a cationic peptide having at least a +2 charge, see claims 5-6. Thus, contrary to Appellant's assertion, Appellant has not indicated that a +2 charge is preferred.

At second paragraph, page 9 to the second paragraph, page 10, and first paragraph page 12, of brief, Appellant argues that Krieg et al. does not teach, disclose or suggest the use of anionic oligonucleotide comprising CpG motifs to form a stabilized immunogen complex with cationic peptide immunogen. Appellant argues that Krieg et al. does not even teach how to select a peptide that is cationic or how to render a peptide cationic by modifying the peptide with addition of lysine, arginine, or histidine at the N- or C-terminal.

Appellant's argument has been considered, however, it is not found persuasive. As mentioned above, while Krieg et al. does not teach a cationic peptide, Krieg et al. clearly teaches that oligonucleotides comprising CpG motifs are immunostimulatory. Krieg et al. also clearly teaches using oligonucleotides comprising CpG motifs as an adjuvant in vaccines and anti-cancer therapeutic agents, including immunotherapeutic agents to enhance the immune response induced by the vaccines and immunotherapeutic agents. Krieg et al. clearly suggests the use of oligonucleotides comprising CpG motifs as adjuvants in vaccines and immunotherapeutic agents. And, at the time the invention was made, Ladd et al. teaches of an immunotherapeutic agent. The immunotherapeutic agent that Ladd et al. teaches is a cationic peptide. The cationic peptide of Ladd et al. has 100% identity to the cationic peptide claimed, and specifically recited in claim 19. The cationic peptide of Ladd et al., which Ladd et al., designates as SEQ ID NO: 35 is the same as claimed SEQ ID NO: 9, which is recited in claim 19. Hence, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to combine the teachings of Krieg et al. and Ladd et al. for the reason(s) set forth in the rejection. Moreover, Appellant is reminded that KRS forecloses argument that specific teaching, suggestion or motivation is required to support a finding of obviousness. *KSR*, 82 USPQ2d at 1396. That is, Krieg et al. does not have to specifically teach or suggest a "cationic peptide" or how to select a peptide that is cationic or how to render the peptide cationic by modifying the peptide to render the claimed invention obvious. In the instant case, it is clear from the teachings of Krieg et al. that oligonucleotides comprising the CpG motifs has

immunostimulatory activities and can be used as adjuvants in vaccines or immunotherapeutic agents.

Additionally, the composition rendered obvious by Krieg et al. and Ladd et al. would necessarily lead to complexation between the anionic oligonucleotide of Krieg et al. and the cationic peptide of Ladd et al. for it is well known that opposite charges, negative and positive, attract one another.

At the last two paragraphs of page 10, and first paragraph page 12, Appellant presented arguments against Ladd et al. Appellant argues that there is no disclosure, teaching or suggestion of complexing the cationic peptide of Ladd et al. with an anionic oligonucleotide comprising the CpG motif. Appellant also argues that there is nothing in Ladd et al. about how to determine whether an oligonucleotide has a negative charge or anything about the charge of the cationic peptide.

Appellant's arguments have been considered, however, it is not found persuasive. It should be noted that had Ladd et al. teaches the complexing the cationic peptide with an anionic oligonucleotide comprising the CpG motif, the Office would have readily applied Ladd et al. as an anticipatory to the claimed invention. However, this is not the case. Ladd et al. is cited, in view of Krieg et al., to have rendered the claimed invention obvious. Ladd et al. teaches an immunotherapeutic agent that is a cationic peptide. The cationic peptide of Ladd et al. has the same sequences as the claimed SEQ ID NO: 9. Krieg et al. teaches an anionic oligonucleotide comprising the CpG motif, and its use as an adjuvant in vaccines and immunotherapeutic agents to enhance the immune response induced by said vaccines and/or immunotherapeutic agents. In

Art Unit: 1645

the instant case, the motivation and suggestion is clearly provided by Krieg et al. Any person of ordinary skill in the art, after reading Krieg et al., would be motivated to combine anionic oligonucleotide of Krieg et al. with the cationic peptide of Ladd et al. to enhance the immune response induced by the cationic peptide of Ladd et al.

Regarding Appellant's assertion that there is nothing in Ladd et al. with respect to the charge of the cationic peptide, it should be noted that Ladd et al. does not have to specifically teach that the peptide disclosed by Ladd et al. is cationic in order to be used as prior art against Appellant's claimed invention. IN the instant case, the cationic peptide of Ladd et al. is inherently cationic. The cationic peptide of Ladd et al. has 100% identity to claimed cationic peptide SEQ ID NO: 9. The fact that Ladd et al. teaches a peptide that is the same as Appellant's cationic peptide establishes a prima facie case that the peptide of Ladd et al. is inherently cationic.

Additionally, with regard to Appellant's argument that there is nothing in Ladd et al. about how to determine whether an oligonucleotide has a negative charge, it is unclear as to the relevance of this argument. In the instant case, Ladd et al. is not the only prior art cited as rendering the claimed invention obvious. The claimed invention is rendered obvious over Krieg et al. in view of Ladd et al.

At second paragraph, page 12 of brief, Appellant argues that the neither Krieg et al. nor Ladd et al. teaches complexation between an anion oligonucleotide with a cationic peptide.

Appellant's argument has been considered, however, it is not found persuasive. Appellant is reminded that the rejection of record is an obviousness rejection of the

claims over Krieg et al., in view of Ladd et al. The rejection of record is not an anticipatory rejection. Had either Krieg et al. or Ladd et al. teaches complexation between an anion oligonucleotide with a cationic peptide, either reference would have been cited as anticipating the claimed rejection. However, such is not the case. The references are cited as rendering the claimed invention obvious.

At paragraphs 3-4, page 12 of brief, Appellant cited *KSR* and appears to argue that the Office used impermissible [*sic*] hindsight.

Appellant's citation of *KSR* and impermissible hindsight has been noted, however, it is not found persuasive. In response to Appellant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, the rejection of record clearly takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Appellant's disclosure, such a reconstruction. Hence, the rejection is deemed proper. With regard to *KSR*, Appellant is reminded that *KSR* forecloses argument that specific teaching, suggestion or motivation is required to support a finding of obviousness. *KSR*, 82 USPQ2d at 1396.

At page 13, Appellant argues that higher titer of antibodies were surprisingly observed.

Appellant's submission has been considered, however, it is not found persuasive. It is not readily apparent why Appellant finds that the attainment of higher titer of antibodies was surprising. Krieg et al. teaches that anionic oligonucleotides have immunostimulatory activities and can be used as adjuvants in vaccines and immunotherapeutic agents to enhance the immune response induced by the vaccine or agent. Thus, use of the anionic oligonucleotide of Krieg et al. with the cationic peptide of Ladd et al. would necessarily result in an enhanced immune response, including higher titer of antibodies produced against the cationic peptide of Ladd et al. In the instant case, the enhancement of immune response noted by Appellant has clearly been predicted and expected by Krieg et al.

Art Unit: 1645

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Emily Le/

Primary Examiner, Art Unit 1648

Conferees:

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648

/Shanon A. Foley/

Supervisory Patent Examiner, Art Unit 1645